REMARKS/ARGUMENTS

Claims 1-77 were pending in the present application before this amendment as set forth above. By this amendment, claims 1, 27, 28, 31, 49, 50, 51, 65, 66 and 76 are amended and claims 26, 40, 41 and 64 are canceled.

In the December 30, 2009 Office Action (hereinafter "Office Action"), the Examiner asserted that claims 1-5, 8-16, 19-22, 33-38, 41-48 and 50-65 were rejected under 35 U.S.C. § 102(a) as being anticipated by U.S. Patent Publication No. 2003/0003571 to Kanegasaki et al. (hereinafter "Kanegasaki"). However, as best understood by Applicant, the Examiner rejected claims 1-7, 9-17, 25, 41-44, 48-63, 71 and 75 under 35 U.S.C. § 102(a) as being anticipated by Kanegasaki. In addition, as best understood by Applicant, the Examiner has not provided any indication of treatment on the merits for any of claims 18, 32 and/or 40. ***Clarification of these rejections is respectfully requested.***

Furthermore, in the Office Action, Claims 9-12 and 57-60 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent No. 6,197,575 to Griffith et al. (hereinafter "Griffith"). Claims 19 and 24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent No. 5,157,438 to Sparks (hereinafter "Sparks"). Further, claims 26-31 and 64-69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent Publication No. 2002/0086280 to Lynes et al. (hereinafter "Lynes"). Still further, claims 26-31 and 64-69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Lynes, and further in view of U.S. Patent No. 6,391,558 to Henkens et al. (hereinafter "Henkens"). Moreover, claims 33-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Lynes, and further in view of U.S. Patent Publication No. 2002/0164816 to Quake (hereinafter "Quake"). Claims 45-46 and 72-73 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent Publication No. 2002/0025547 to Rao (hereinafter "Rao"). In addition, claims 47 and 74 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent No. 6,168,948 to Anderson et al. (hereinafter "Anderson"). Also, claim 76 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of U.S. Patent Publication No. 2001/0044143 to Herman et al. (hereinafter "Herman"). Further, claim 77 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki,

in view of Herman, and further in view of U.S. Patent No. 5,624,537 to Turner et al. (hereinafter "Turner"). The Examiner also objected to claims 40 and 41 as being of improper dependent form.

Applicant very much appreciates the Examiner's careful review of the instant application.

In response, as set forth above, claims 1, 27, 28, 31, 49, 50, 51, 65, 66 and 76 have been amended for better form. For example, features of originally filed claim 26, now canceled, have been incorporated into amended claim 1, and features of originally filed claim 64, now canceled, have been incorporated into amended claim 49. In addition, without acquiescing to the propriety of the Examiner's rejections, claims 26, 40, 41 and 64 have been canceled without prejudice, which makes the Examiner's rejections under 35 U.S.C. § 102 and 35 U.S.C. § 103 moot. Applicant reserves every right in these canceled claims to file continuation/divisional applications.

Support for the amendments can be found in the disclosure as originally filed, for example in the claims as originally filed, in paragraphs from page 20, lines 17-31 through page 29, lines 1-13 of the specification and in Figs. 1-5 of the drawings. Applicant submits that no new matter has been added.

Any amendments to the claims not specifically referred to herein as being included for the purpose of distinguishing the claims from cited references are included for the purpose of clarification, consistence and/or grammatical correction only.

It is now believed that the application is in condition for allowance at least for the reasons set forth below and such allowance is respectfully requested.

The following remarks herein are considered to be responsive thereto.

Rejections under 35 U.S.C. § 102(a)

In the Office Action, as best understood by Applicant, claims 1-7, 9-17, 25, 41-44, 48-63, 71 and 75 were rejected under 35 U.S.C. § 102(a) as being anticipated by Kanegasaki. Applicant respectfully traverses these rejections for at least the reasons set forth below:

Claims 1-25, 27-39 and 42-48 :

As set forth above, amended claim 1 recites "[a] bioreactor comprising:

(a) a substrate having a first surface and an opposite second surface, defining a channel therein;

(b) a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end; and

(c) ***means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers.***" (Emphasis added.)

As stated in MPEP § 2131, a claim is anticipated under 35 U.S.C § 102(a) ***only if each and every element as set forth in the claim is found in a single prior art reference.***

As described on page 23, lines 5-30 to page 25, lines 1-3, and on page 26, lines 7-31 to page 27, lines 1-5 of the specification as originally filed and as shown in Figs. 1A and 1B of the drawings as originally filed, in one exemplary embodiment of the present invention, a bioreactor 200 includes a substrate 230 having a first surface and an opposite second surface. The bioreactor 200 has a plurality of arrays of chambers 204 formed on the substrate 230. Each array of chambers 204 is adapted for receiving cells in a liquid medium and includes a channel 202 and a plurality of chambers 206 formed in the substrate 230. Each of the plurality of chambers 206 is adapted for receiving cells in a liquid medium and formed with an open end 262, an opposite closed end 264 and sidewalls 266. The open end 262 and the closed end 264 of a particular chamber 206 define a depth, d, therebetween for the corresponding chamber 206, which is in fluid communication with the channel 202 through the open end 262. Additionally, the sidewalls 266 defines a width, w, therebetween for the corresponding chamber 206. The bioreactor 200 also includes ***means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers 206. In one embodiment, the means for electrochemical measurements includes a counter electrode 211, a reference electrode 212, and a plurality of electrically conductive leads.***

In contrast, as understood by Applicant, Kanegasaki discloses "a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [0009].) In one embodiment as shown in Fig. 3, for example, a "well unit [including a substrate 7 and a substrate 8] has a channel 1 and wells 2A and 2B in which a sample such as a cell suspension or a specimen solution is contained. A sample is supplied into the well 2A or 2B through a tube 3A or 3B with the use of a micropipette, etc. After [cell] migration, cells are collected from the well 2A or 2B through the tube 3A or 3B." (Kanegasaki, [0088].) Kanegasaki discloses that "[f]or detection in integrated [well] units, ***it is preferable*** to employ a system wherein the channels of the units are successively scanned along with ***an objective lens [(i.e. using optical detection)]***." (Kanegasaki, [0162] - [0165].) (Emphasis added.) In other words, Kanegasaki does not disclose, teach, or suggest a bioreactor having "a substrate having a first surface and an opposite second surface, defining a channel therein; a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls…and ***means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers***" and having all of the other features recited in amended claim 1. (Emphasis added.)

Therefore, Kanegasaki does not disclose, teach, or suggest a bioreactor having all of the features recited in amended claim 1. For at least these reasons, Applicant submits that claim 1, as amended, is not anticipated by Kanegasaki and is patentable under 35 U.S.C. § 102(a) over Kanegasaki.

Accordingly, claims 2-25, 27-39 and 42-48, which depend from now allowable claim 1, are also patentable under 35 U.S.C. § 102(a) over Kanegasaki for at least this reason.

Claims 2-25, 27-39 and 42-48 also contain additional patentable subject matter. For example, originally filed claim 8 discloses a bioreactor having "a barrier for at least one of the chambers, wherein the barrier is positioned at the open end of the corresponding chamber and ***has a porosity to allow the corresponding chamber and the channel in fluid communication and allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate***

between the corresponding chamber and the channel." (Emphasis added.) In contrast, as understood by Applicant, Kanegasaki discloses ***grooves or terraces***, for example, grooves 5 on a bank 10 in a channel 1 (see, e.g. Figs. 2, 4 and 6). Kanegasaki does not disclose, teach, or suggest a bioreactor having these features of claim 8, taken alone or in combination with the features recited in amended claim 1. Accordingly, individual consideration and allowance of each claim is respectfully requested.

Claims 49-63 and 65-75:

As set forth above, amended claim 49 recites "[a] bioreactor comprising:

(a) a substrate having a first surface and an opposite second surface; and

(b) a plurality of array of chambers formed on the substrate, each being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, and wherein at least two of the plurality of chambers have depths same or different from each other; and

for at least one array of chambers, further comprising means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers. (Emphasis added.)

Incorporating herewith the reasons set forth above why amended claim 1 is patentable under 35 U.S.C. § 102(a) over Kanegasaki, Applicant submits that claim 49, as amended, is patentable under 35 U.S.C. § 102(a) over Kanegasaki for at least these reasons.

Accordingly, claims 50-63 and 65-75, which depend from now allowable amended claim 49, are also patentable under 35 U.S.C. § 102(a) over Kanegasaki for at least this reason.

Claims 50-63 and 65-75 also contain additional patentable subject matter. For example, originally filed claim 56 discloses a bioreactor having "for at least one array of chambers, …a

barrier for at least one of the chambers, wherein the barrier is positioned at the open end of the corresponding chamber and ***has a porosity to allow the corresponding chamber and the channel in fluid communication and allow at least one predetermined type of cells to permeate between the corresponding chamber and the channel and at least another predetermined type of cells not to permeate between the corresponding chamber and the channel.***" (Emphasis added.) In contrast, as set forth above and as understood by Applicant, Kanegasaki discloses ***grooves or terraces***, for example, grooves 5 on a bank 10 in a channel 1 (see, e.g. Figs. 2, 4 and 6). Kanegasaki does not disclose, teach, or suggest a bioreactor having these features of claim 56, taken alone or in combination with the features recited in amended claim 49 and/or any of the intervening claims. Accordingly, individual consideration and allowance of each claim is respectfully requested.

Rejections under 35 U.S.C. § 103(a)

In the Office Action, claims 9-12 and 57-60 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Griffith. Claims 19 and 24 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Sparks. Further, claims 26-31 and 64-69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Lynes. Still further, claims 26-31 and 64-69 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Lynes, and further in view of Henkens. Moreover, claims 33-39 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Lynes, and further in view of Quake. Claims 45-46 and 72-73 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Rao. In addition, claims 47 and 74 were rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Anderson. Also, claim 76 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Herman. Further, claim 77 was rejected under 35 U.S.C. § 103(a) as being unpatentable over Kanegasaki, in view of Herman, and further in view of Turner. Applicant respectfully traverses these rejections for at least the reasons set forth below:

Claims 2-25, 27-39 and 42-48, and 65-75:

Kanegasaki, as understood by Applicant, discloses "a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [0009].) Lynes, as understood by Applicant, discloses a "system for monitoring cell movement in response to chemotactic and chemokinetic factors" that is "capable of measuring changes in impedance and other electrical parameters." (Lynes, Abstract.) Henkens, as understood by Applicant, discloses a "system [that] utilizes biological probes such as nucleic acid or peptide nucleic acid probes which are complementary to and specifically hybridize with selected nucleic acid segments in order to generate a measurable current when an amperometric potential is applied." (Henkens, Abstract.) Quake, as understood by Applicant, discloses "microfluidic chromatography devices for separating an analyte from a sample solution, and methods for producing and using the same." (Quake, Abstract.) Rao, as understood by Applicant, discloses a "bioprocessing system (and technique) [that] relies on non-invasive optical chemical sensing technology wherein an optical excitation source excites an optical chemical sensor." (Rao, Abstract.) Anderson, as understood by Applicant, discloses "a miniaturized integrated nucleic acid diagnostic device and system which includes a nucleic acid extraction zone including nucleic acid binding sites." (Anderson, Abstract.)

As set forth above, claims 2-25, 27-39 and 42-48, which depend from now allowable amended claim 1, are patentable under 35 U.S.C. § 102(a) over Kanegasaki for at least this reason. Accordingly, these claims are also patentable under 35 U.S.C. § 103(a) over any combination of the Kanegasaki, Lynes, Henkens, Quake, Rao, and/or Anderson for at least this reason.

In addition, as set forth above, claims 50-63 and 65-75, which depend from now allowable amended claim 49, are also patentable under 35 U.S.C. § 103(a) over any combination of Kanegasaki, Lynes, Henkens, Quake, Rao, and/or Anderson for at least this reason.

Claim 26:

As set forth above, features of originally filed claim 26 have been incorporated into amended claim 1 and claim 26 has been canceled accordingly, which makes the Examiner's rejection under 35 U.S.C. § 103(a) moot. However, even assuming that this rejection were not rendered moot for this reason, Applicant submits that claim 26, as originally filed, would be allowable over any combination of Kanegasaki and/or Lynes for at least the following reasons:

As set forth above and as understood by Applicant, Kanegasaki discloses "a well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [0009].) Kanegasaki discloses that "[f]or detection in integrated [well] units, ***it is preferable*** to employ a system wherein the channels of the units are successively scanned along with ***an objective lens***" and/or using a CCD camera or CCD video camera, ***i.e. using optical detection.*** (Kanegasaki, [0162] - [0165].) (Emphasis added.) As conceded by the Examiner on page 6 of the Office Action, Kanegasaki does not disclose a means for electrochemical measurements.

Lynes, as understood by Applicant, discloses a "system for monitoring cell movement in response to chemotactic and chemokinetic factors" that is "capable of measuring changes in impedance and other electrical parameters." (Lynes, Abstract.) On page 6 of the Office Action, the Examiner asserts that it would have been obvious to combine the Kanegasaki and Lynes references since "automated detection using impedance measurements is often times ***superior to visual [(i.e. optical)] observation***, ***which is difficult and laborious***." (Emphasis added.) However, in direct contrast and as set forth above, Kanegasaki instead specifically discloses ***a preference for optical detection***. Thus, for at least these reasons, Kanegasaki ***teaches away*** from the proposed combination with Lynes.

Therefore, neither Kanegasaki nor Lynes, taken alone or in combination, disclose, teach, or suggest a bioreactor comprising "means adapted for electrochemical measurements of the cells responsive to the liquid medium in at least one of the chambers" and having all of the other features recited in originally filed claim 26. For at least these reasons, even assuming that claim 26 had not been canceled and the rejection under 35 U.S.C. § 103(a) thereby made moot, Applicant submits that originally filed claim 26 would be patentable under 35 U.S.C. § 103(a)

over Kanegasaki and/or Lynes.

Claim 64:

As set forth above, features of originally filed claim 64 have been incorporated into amended claim 49 and claim 64 has been canceled accordingly, which makes the Examiner's rejection under 35 U.S.C. § 103(a) moot. However, even assuming that this rejection was not rendered moot for this reason, Applicant submits that claim 64, as originally filed, would be allowable over any combination of Kanegasaki and/or Lynes for at least the reasons set forth above why amended claim 26 would be patentable under 35 U.S.C. § 103(a) over Kanegasaki and/or Lynes.

Claims 76 and 77:

As set forth above, amended claim 76 recites "[a] method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of:

(i) providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate, each being adapted for receiving cells in a liquid medium and comprising a channel and a plurality of chambers formed in the substrate, wherein each of the plurality of chambers is adapted for receiving cells in a liquid medium and formed with an open end, an opposite closed end and side walls, the open end and the closed end defining a depth, d, therebetween for the corresponding chamber, the sidewalls defining a width, w, therebetween for the corresponding chamber, and the chamber being in fluid communication with the channel through the open end, and wherein at least two of the plurality of chambers have depths different from each other; and

(ii) ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor.***" (Emphasis added.)

In contrast, as set forth above and as understood by Applicant, Kanegasaki discloses "a

well unit to be used in an apparatus whereby movements of cells based on their own actions can be accurately and easily detected, in case of detecting the chemotaxis of cells due to a chemotactic factor or the inhibition of the chemotaxis of cells by an inhibitor." (Kanegasaki, [0009].) On page 9 of the Office Action, the Examiner concedes that "Kanegasaki does not disclose the use of biofilms." In other words, Kanegasaki does not disclose, teach, or suggest a method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of "providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate…and ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor***" as recited in amended claim 76. (Emphasis added.)

Herman, as understood by Applicant, discloses "methods and devices in which living cells or subcellular biocatalysts are immobilized in an open chamber defined by two rotating disks." (Herman, Abstract.) Herman does not disclose, teach, or suggest a method for ***culturing a plurality of biofilms***, each containing a predetermined type of cells or cell growth conditions, comprising the steps of "providing a bioreactor that has a substrate having a first surface and an opposite second surface and a plurality or array of chambers formed on the substrate…and ***culturing at least two biofilms in at least two arrays of chambers of the bioreactor***" as recited in amended claim 76. (Emphasis added.)

Turner, as understood by Applicant, discloses "a regenerable biosensor probe adapted for positioning in a bioreactor." (Turner, Abstract.)

For at least the reasons set forth above, Applicant respectfully submits that the Examiner has failed to make a *prima facie* case to support the rejection of claim 76 under 35 U.S.C. §103(a) over Kanegasaki and/or Herman. First, there is no suggestion or motivation to modify the references or combine the reference teachings. Second, there is no reasonable expectation of success of combining the reference teachings. Finally, the combination of references does not teach or suggest all elements of Applicant's claims.

In supporting the obviousness rejections under 35 U.S.C. §103, the Examiner "bears ***the initial burden…of presenting a prima facie case of unpatentability***…After evidence or argument is submitted by the applicant in response, patentability is determined ***on the totality of the record***." *Ex parte Wada and Murphy*, BPAI Appeal No. 2007-3733 (January 14, 2008), and

"***Office personnel must articulate***", among other things, "***a finding that the prior art included each element claimed*** ...", MPEP 2143 (A)(1). The "***unwitting application of hindsight" is inappropriate***. *Ex parte So and Thomas*, BPAI Appeal No. 2007-3967 (January 4, 2008). In other words, the Examiner's "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). (MPEP § 2142). (Emphasis added.)

For at least the foregoing reasons, Applicant respectfully submits that claim 76, as amended, is patentable under 35 U.S.C. §103(a) over any combination of Kanegasaki and/or Herman.

Accordingly, claim 77, which depends from now allowable amended claim 76, is also patentable under 35 U.S.C. § 103(a) over any combination of Kanegasaki, Herman, and/or Turner for at least this reason.

Claim Objections

In the Office Action, the Examiner objected to claims 40 and 41 as being of improper dependent form for failing to further limit the subject matter of a previous claim. Specifically, the Examiner asserted that "[c]laims 40 and 41 duplicate claims 31 and 32 and therefore, do not further limit claim 28." In response, as set forth above, claims 40 and 41 have been canceled without prejudice, which renders these objections moot.

CONCLUSION

Applicant respectfully submits that the foregoing Response places this application in condition for allowance. If the Examiner believes that there are any issues that can be resolved by a telephone conference, or that there are any informalities that can be corrected by an Examiner's amendment, to facilitate the prosecution, please call the undersigned at 404.495.3678. No fee is due, but the Commissioner is hereby authorized to charge any petition fee under 37 CFR 1.17(f),(g) or (h) or any deficiency of fees and credit of any overpayments to Deposit Account No. 50-3537.

Respectfully submitted,

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